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EXAMINER	
RAGHU, GANAPATHIRAM	
ART UNIT	PAPER NUMBER
1652	

MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/855,320	BAYER, ROBERT	
	Examiner	Art Unit	
	Ganapathirama Raghu	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 June 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *107 and 108* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *107 and 108* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Application Status

Please note that the instant application/case has been transferred to examiner Ganapathirama Raghu, Art Unit 1652, whose telephone number is (571)-272-4533 and all further enquiries regarding this application should be directed to said examiner.

In response to the Office Action mailed on 12/18/2006, applicants' filed a response on 06/18/2007. Examiner notes that on the face of the amended claims document the Application No. is denoted as 10/198,806, however the claims and amendments are directed to the instant application 09/855,320. Said response, canceled claims 1-4, 6, 8, 10-17, 19-36, 38, 40, 42-49, 51, 52, 54, 55, 87-89, 91, 93, 95-102 and 104 and added new claims 107 and 108. Thus claims 107 and 108 are pending in this application and are under consideration.

Objections and rejections not reiterated from previous action are hereby withdrawn.

Claim Objections

Claim 108 is objected to because of the following informalities: Line 3 in Claim 108 is blank and line 4 does not end with a period. Appropriate correction is required.

Maintained-Claim Rejections: 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Enablement

Claims 107 and 108 are rejected under 35 U.S.C. 112, first paragraph. The prior art enables a method of modifying the fucosylation pattern of a recombinant glycopeptide comprising an acceptor moiety for a recombinant eukaryotic FucT-VI or FucT-VII fucosyltransferase, said method comprising contacting said recombinant glycopeptide with a

reaction mixture comprising a fucose donor moiety and a eukaryotic FucT-VI or FucT-VII fucosyltransferases as taught by the combination of Palcic (1989) or Ichikawa et al., (1992) and in view of Weston et al., (1992) and Kimura et al., (1999) (see below for the rejection under 35 U.S.C. 103(a)). However, the specification does not reasonably provide enablement for any method of modifying the fucosylation pattern of a recombinant glycopeptide comprising an acceptor moiety for any recombinant eukaryotic FucT-VI or FucT-VII fucosyltransferase, said method comprising contacting said recombinant glycopeptide with a reaction mixture comprising a fucose donor moiety and any eukaryotic FucT-VI or FucT-VII fucosyltransferases. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and or use the invention commensurate in scope with the claims.

Factors to be considered in determining whether undue experimentation is required are summarized in *In re Wands* (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Claims 107 and 108 are so broad as to encompass for any method of modifying the fucosylation pattern of a recombinant glycopeptide comprising an acceptor moiety for any recombinant eukaryotic FucT-VI or FucT-VII fucosyltransferase, said method comprising contacting said recombinant glycopeptide with a reaction mixture comprising a fucose moiety and any eukaryotic FucT-VI or FucT-VII fucosyltransferases. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large

number of polypeptides to be used in said method of modifying the fucosylation pattern of a recombinant glycopeptide as broadly encompassed by the claims. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires knowledge and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the encoded proteins' structure relates to its function. However, in this case the disclosure is limited to modifying the fucosylation pattern of a recombinant glycopeptide, said method as taught in the prior art i. e., see the rejection below under 35 U.S.C. 103(a). In view of the great breadth of the claims, amount of experimentation required to make the claimed polypeptides and encoding polynucleotides, the lack of guidance, working examples, and unpredictability of the art in predicting function from a polypeptide primary structure (for example, see Whisstock et al., Prediction of protein function from protein sequence and structure. Q Rev Biophys. 2003, Aug. 36 (3): 307-340. Review), to practice the claimed invention would require undue experimentation. As such, the specification fails to teach one of ordinary skill how to make and use the full scope of the polypeptides recited by the claimed methods.

While enzyme isolation techniques, recombinant and mutagenesis techniques are known, and it is not routine in the art to screen for multiple substitutions or multiple modifications as encompassed by the instant claim, the specific amino acid positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such

modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions or deletions.

The specification does not support the broad scope of the claims which encompass for any method of modifying the fucosylation pattern of a recombinant glycopeptide comprising an acceptor moiety for any recombinant eukaryotic FucT-VI or FucT-VII fucosyltransferase, said method comprising contacting said recombinant glycopeptide with a reaction mixture comprising a fucose donor moiety and any eukaryotic FucT-VI or FucT-VII fucosyltransferases., because the specification does not establish: (A) regions of the protein structure of any FucT-VI or FucT-VII fucosyltransferase which may be modified without affecting the activity of fucosyltransferase polypeptide having specific activity and biochemical characteristics such as synthetic and hydrolytic activities; (B) the general tolerance of the fucosyltransferase polypeptide having specific activity and biochemical characteristics to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any amino acid residue or the respective codon in the polynucleotide with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claim broadly including any method of modifying the fucosylation pattern of a recombinant glycopeptide comprising an acceptor moiety for any recombinant eukaryotic FucT-VI or FucT-VII fucosyltransferase, said method comprising contacting said recombinant

glycopeptide with a reaction mixture comprising a fucose donor moiety and any eukaryotic FucT-VI or FucT-VII fucosyltransferases, said method comprising contacting said glycoprotein with a genus of polypeptides including mutants, variants and recombinants having fucosyltransferase activity with an enormous number of modifications. The scope of the claim must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of any method of modifying the fucosylation pattern of a recombinant glycopeptide comprising an acceptor moiety for any recombinant eukaryotic FucT-VI or FucT-VII fucosyltransferase, said method comprising contacting said recombinant glycopeptide with a reaction mixture comprising a fucose donor moiety and any eukaryotic FucT-VI or FucT-VII fucosyltransferases, said method comprising contacting said glycoprotein with a genus of polypeptides including mutants, variants and recombinants having fucosyltransferase activity with an enormous number of modifications is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

In support of their request that the prior rejection of claims 107 and 108, under 35 U.S.C. 112, first paragraph be withdrawn, applicants' provide the following arguments. These arguments are relevant to the new rejection explained above.

(A) The new claims recite only FucT-VI or FucT-VII fucosyltransferase.

(B) The specification teaches FucT-VI or FucT-VII fucosyltransferase in pages 26-28, provides suitable substrates for these enzymes in pages 20-22, suitable acceptor moieties on pages 28-29 and a suitable methods of glycosylating a glycoprotein using a mutant endoglycanase in pages

37-38 and working examples (Example 2 and 3) and methods of assessing fucosylation patterns of glycopeptides are described in page 33.

(C) The level of unpredictability in the field does not rise to the level of requiring undue experimentation.

These arguments are not found to be persuasive for the following reasons.

(A) Reply: Examiner acknowledges the new claims are directed only to FucT-VI or FucT-VII fucosyltransferase, however claims as written encompass any eukaryotic FucT-VI or FucT-VII fucosyltransferase, without reference to a specific parent sequence, it would not be clear to a skilled artisan which of the infinite number of parent FucT-VI or FucT-VII fucosyltransferases and their mutants, variants and recombinants are encompassed in the claims. The broadest interpretation of claims encompasses a genus of mutant polypeptides having FucT-VI or FucT-VII fucosyltransferase activity with any structure and clearly constitutes undue experimentation as it would involve making and testing many parent sequences including the mutants, variants and recombinants of said parent sequences.

(B) and (C) Reply: Examiner would like to acknowledge the substrates are known and the methods for analysis of glycosylation patterns are known in the art. As indicated in the above reply for (A), the specification fails to enable the skilled artisan to know which of the large number of possible parent sequences including their mutants, variants and recombinants have the desired characteristics. Moreover, it would be undue experimentation for a skilled artisan, as the skilled artisan would be required to make and test an essentially unlimited number of mutants, variants and recombinants. Examiner would like to reiterate that to determine the effect of structural modification on the fucosylation activity of any fucosyltransferase, a skilled artisan

should be provided with details and guidance regarding the how the structure of any fucosyltransferase is correlated with its activity.

For these reasons, claims 107 and 108 are rejected under 35 U.S.C. 112, first paragraph for enablement.

Written description

Claims 107 and 108 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not disclosed in the specification in such a way as to reasonably convey to one of skilled in the relevant art that the invention(s), at the time the application was filed, had possession of the claimed invention.

Claims 107 and 108 are directed to a method of modifying the fucosylation pattern of a recombinant glycopeptide comprising an acceptor moiety for a recombinant eukaryotic FucT-VI or FucT-VII fucosyltransferase, said method comprising contacting said recombinant glycopeptide with a reaction mixture comprising a fucose moiety and a genus of eukaryotic FucT-VI or FucT-VII fucosyltransferases. The recited method of modifying the fucosylation pattern of a recombinant glycopeptide comprises using a genus of polypeptides and the claimed genus is large and variable with the potentiality of many different structures including variants, mutants and recombinants of FucT-VI or FucT-VII fucosyltransferases and from very many different sources. Therefore, many structurally distinct polypeptides are used within the scope of the methods of the claims. The specification only discloses use of FucT-VI or FucT-VII, exemplary examples in Examples 2 and 3 on pages 44-45 of what is known in the art, however no species (structure associated with function) of the recited genus of polypeptides in a method of modifying the fucosylation pattern of a recombinant glycopeptide comprising an acceptor

moiety for a recombinant eukaryotic FucT-VI or FucT-VII fucosyltransferase, said method comprising contacting a full-length recombinant glycopeptide with a reaction mixture comprising FucT-VI or FucT-VII fucosyltransferase and a fucose donor moiety has been disclosed.

Therefore, one skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed. Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

In support of their request that the prior rejection of claims 107 and 108 for insufficient written description be withdrawn, applicants', provide the following argument, which are relevant to the above rejection.

"Specification provides ample written description for use of a FucT-VI or FucT-VII fucosyltransferase in fucosylating a glycopeptide including working examples (Examples 2 and 3)..."

The argument is not found to be persuasive for the following reasons.

(A) Reply: Examiner acknowledges, the specification only discloses exemplary examples in Examples 2 and on pages 44-45 of what is known in the art, however no species (structure associated with function) of the recited genus of polypeptides in a method of modifying the fucosylation pattern of a recombinant glycopeptide comprising an acceptor moiety for a recombinant eukaryotic FucT-VI or FucT-VII fucosyltransferase, said method comprising contacting said recombinant glycopeptide with a reaction mixture comprising a fucose donor

moiety and a eukaryotic FucT-VI or FucT-VII fucosyltransferase has been disclosed. Therefore, without reference to a specific parent sequence, it would not be clear to a skilled artisan which of the infinite number of parent FucT-VI or FucT-VII fucosyltransferases and their variants, mutants and recombinants are encompassed in the claims.

Claim Rejections 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 107 and 108 are rejected under 35 U.S.C. 103(a) as being unpatentable over Palcic (1989) or Ichikawa et al., (1992) and in view of Weston et al., (1992) and Kimura et al., (1999) (all the cited references are in IDS under prior art references). Palcic (1989, Abstract and entire document) or Ichikawa et al., (1992, Abstract and entire document) disclose the chemical and enzymatic synthesis of glycopeptides (Sialyl Lewis x derivatives; Palcic) and oligosaccharides terminating in tumor-associated Sialyl Lewis a determinant (Ichikawa et al.,). However Palcic (1989) or Ichikawa et al., (1992) are silent regarding specific recombinant eukaryotic FucT-VI or FucT-VII fucosyltransferase in said methods. Weston et al., (1992)

teaches molecular cloning of human FucT-VI fucosyltransferase (Abstract section) including substrate specificity such as donor and acceptor moieties, optimal reaction conditions and fuosyltransferase assays (Experimental procedures, pages 24576- 24577). Kimura et al., (1999) teaches molecular cloning of human FucT-VII fucosyltransferase (Abstract section) including substrate specificity such as donor and acceptor moieties, and fucosylation patterns catalyzed by said enzyme (Results, pages 4531- 4533, Fig. 1). It would have been obvious to a person of ordinary skill in the art to use the FucT-VI or FucT-VII fucosyltransferase of Weston et al., (1992) and Kimura et al., (1999) in a method of modifying the fucosylation pattern of a recombinant glycopeptide comprising an acceptor moiety for a recombinant eukaryotic FucT-VI or FucT-VII fucosyltransferase, said method comprising contacting said recombinant glycopeptide with a reaction mixture comprising a donor moiety and a eukaryotic FucT-VI or FucT-VII fucosyltransferases as taught by the combination of Palcic (1989) or Ichikawa et al., (1992). Motivation to do so derives from the fact that production of different forms of glycoproteins comprising desired oligosaccharides with desired properties are useful in pharmaceutical industry for various clinical applications (Palcic or Ichikawa et al.,). The expectation of success is high, because Weston et al., (1992) and Kimura et al., (1999) teach recombinant eukaryotic FucT-VI or FucT-VII fucosyltransferase and Palcic (1989) or Ichikawa et al., (1992) disclose fucosylating glycoproteins and employing fucosyltransferases to achieve desired patterns of fucosylation in glycoproteins of interest. Therefore, 107 and 108 are rejected under 35 U.S.C. 103(a) as being unpatentable over Palcic (1989) or Ichikawa et al., (1992) and in view of Weston et al., (1992) and Kimura et al., (1999).

Summary of Pending Issues

The following is a summary of issues pending in the instant application.

1) Claim 108 is objected to due to informalities.

2) Claims 107 and 108 are rejected under 35 U.S.C. 112, first paragraph for enablement and written description.

3) Claims 107 and 108 are rejected under 35 U.S.C. 103(a) as being unpatentable over Palcic (1989) or Ichikawa et al., (1992) and in view of Weston et al., (1992) and Kimura et al., (1999) (all the cited references are in IDS under prior art references).

Conclusion

None of the claims are allowable. Claims 107 and 108 are rejected/objected for the reasons identified in the Rejections and Summary sections of this Office Action. Applicants must respond to the objections/rejections in each of the sections in this Office Action to be fully responsive for prosecution.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period

will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Final Comments

To insure that each document is properly filed in the electronic file wrapper, it is requested that each of amendments to the specification, amendments to the claims, Applicants' remarks, requests for extension of time, and any other distinct papers be submitted on separate pages.

It is also requested that Applicants identify support, within the original application, for any amendments to the claims and specification.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ganapathirama Raghu whose telephone number is 571-272-4533. The examiner can normally be reached between 8 am-4: 30 pm EST. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on 571-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300 for regular communications and for After Final communications. Any inquiry of a general nature or relating to the status of the application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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Patent Examiner
Art Unit 1652
Sept. 12 2007.

/Rebecca Prouty/
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